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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/753,752	SHORT, JAY M.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/29/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Application

Claims 1-5 are pending.

Applicant's amendment of claims 1-3 and addition of claims 4-5 in Paper No. 11, filed on 4/29/2003 is acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Terminal Disclaimer

1. The terminal disclaimer filed on 4/29/2003 does not comply with 37 CFR 1.321(b) and/or (c) because:

> The application/patent being disclaimed has been improperly identified since the number used to identify the application being disclaimed is incorrect. The correct number is 09/753,752 and not 09/467,740 as written.

Drawings

2. The drawings submitted on 4/29/2003 have been reviewed and are approved by a draftsperson under 37 CFR 1.84 or 1.152.

Claim Objections

3. Claim 3 is objected to because of the following informalities: for clarity, it is suggested that the term "in liquid phase assay" be replaced with "in a liquid phase assay". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 3-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 3 (claims 4-5 dependent thereon) is indefinite in the recitation of "screening for a specified enzyme characteristic in a library of clones prepared by (i).....(ii), and (iii) expressing the library of clones..." for the following reasons. The term "library of clones prepared by" implies that the steps described immediately after are related to the preparation of the library. However it is unclear as to how step (iii) can be part of the preparation process if step (iii) refers to how the clones will be used after they are made. It is suggested that the claim be amended to recite "screening for a specified enzyme characteristic in an expression product prepared by (i).....". For examination purposes, the suggested language will be used. Correction is required.

7. Claim 5 is indefinite in the recitation of "wherein the specified enzymatic characteristic is selected from pH stability, temperature stability" for the following reasons. pH stability and temperature stability are not properties which are only found in enzymes. Since the protein recited in claim 3 can be any protein and not just an enzyme, it is unclear as to how pH stability and temperature stability can be considered "enzymatic characteristics". For examination purposes, the term "specific enzymatic characteristics" will be interpreted as "specific characteristics". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

10. This rejection, which has been discussed at length in Paper No. 9, mailed on 12/27/2002, was applied to claims 1-3 and is now applied to newly added claims 4-5 for the reasons of record.

11. Applicants argue that claims 1-3 have been limited to enzyme characteristics. Furthermore, Applicants argue that the example described in the specification was merely an illustration of the invention and not the sole embodiment of the invention and that it is settled law that Applicant's claims should not be limited to the scope of the examples. In addition, Applicants submit that the teachings of the specification are also supplemented by the knowledge of the art and that at the time the invention was filed, enzyme assays were well known for many enzymatic activities. Applicants argue that the Examiner has provided no support to the conclusion that one of skill in the art would not know how to discount false positives, and that the Examiner's assertion that heating a cell sample to 70 C would in many cases inactivate the molecule being tested seems to ignore the fact that if the recombinant enzyme is inactivated, that

would not provide the information the method is meant to provide. According to Applicants, when the recombinant enzyme to be detected is not functional at 70 C, one could use the technique of subtracting host cell molecules. In addition, Applicants submit that claim 3 as amended now requires that the DNA to be used for the preparation of clones be selected by recovering those DNAs that hybridize to probes containing a full-length or a segment of a polynucleotide encoding a desired enzyme, therefore reducing the number of clones to be subtracted.

12. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. The Examiner acknowledges that claims 1-2 are now limited to enzymes, however claims 3-5 are not limited to enzymes, as indicated above in claims rejections under 35 USC 112 second paragraph. Furthermore, while the Examiner acknowledges that (1) it is settled law that Applicant's claims do not have to be limited to the scope of the examples, (2) enzyme assays for many enzyme activities were known at the time of filing, and (3) the E. coli genome was known at the time of filing, the Examiner disagrees with Applicant's contention that the claimed invention is adequately described. The claimed invention as it relates to claims 3-5 is still drawn to a method which screens for any protein characteristic. Furthermore, it is noted that the method as claimed is not limited to the use of E. coli as the host cell used in the preparation of clones. As such, any organism can be used as a host cell. Therefore, while it is agreed that the E. coli genome was known at the time of filing, it is unclear as to how "subtraction" as indicated by Applicants in the instant Response is described for other organisms for which their corresponding genomes are unknown.

In regard to Applicant's disagreement with the Examiner's conclusions in regard to "false positives" and the inactivation of the molecules being tested at 70 C, it is noted that the claims have been interpreted in light of the specification. As such, the Examiner has considered the examples provided by Applicants for reduction to practice of the claimed invention. While one could argue that the method is adequately described since one can use it to identify clones which express a polynucleotide encoding a unique enzymatic activity not shared by any enzyme endogenously produced by the host cell, the examples provided in the specification and the scope of the claims as written indicate that the host cell may express enzymes which have similar properties to those being identified in the method. In fact, this is evidenced by the fact that the specification teaches heating of E. coli clones to 70 to inactivate E. coli (host cell) enzymes. As such, while the specification discloses one method to discard false positives, i.e. heating to 70 C for 45 minutes to kill E. coli cells, and the detection of hydrolase enzymatic activity which is measurable after heating, there is no other method described in the specification to discard false positives if the enzymatic activity being tested is heat-sensitive. Applicant's arguments in regard to how to practice the claimed method when the enzymatic activity is heat-sensitive are not persuasive since, as indicated above, the scope of the claims encompasses any host cell and the genomes required to practice the method as indicated in the Response have not been described. Therefore, in view of the information provided and for the reasons set forth above and in Paper No. 9, one cannot reasonably conclude that the claimed invention is adequately described.

13. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying E. coli clones of a recombinant DNA library

derived from an uncultivated microorganism wherein the clones are screened for hydrolase activity after heating to 70 C, does not reasonably provide enablement for a method of identifying clones of a recombinant DNA library derived from an uncultivated microorganism wherein the clones are tested for expression of any enzyme having any enzymatic characteristic or any protein having any characteristic. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

14. This rejection, which has been discussed at length in Paper No. 9, mailed on 12/27/2002, was applied to claims 1-3 and is now applied to newly added claims 4-5 for the reasons of record.

15. Applicants argue that the comments above in regard to the high level of skill in the art and how the knowledge of the art is deemed to supplement the specification apply equally to the instant rejection. Applicants submit that the claims have been amended to recite that the molecules screened are enzymes, therefore the Examiner's assertion that the specification is not enabling for the full scope of the claims is now obviated. It is Applicant's contention that one of skill in the art can practice the claimed invention without undue experimentation.

16. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. As indicated above, while it is agreed that claims 1-2 are now limited to enzymes, claims 3-5 are still drawn to any protein. The Examiner disagrees with Applicant's contention that the claimed invention is enabled due to the high level of skill in the art and how the knowledge of the art is deemed to supplement the specification for the reasons set forth

above. Therefore, one of skill in the art cannot reasonably conclude that the specification is enabling for the full scope of the claimed invention.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yen et al. (US Patent No. 5171684, 1992) in view of More et al. (Appl. Environ. Microbiol. 60(5):1572-1580, 1994).

19. This rejection, which has been discussed at length in Paper No. 9, mailed on 12/27/2002, was applied to claims 1-3 and is now applied to newly added claims 4-5 for the reasons of record.

20. Applicants argue that claim 1 as amended is not anticipated by the cited references since claim 1 requires screening in the liquid phase a library of expression clones randomly produced from DNA of at least one uncultivated microorganism, wherein said screening is to identify clones which express an enzyme with a desired characteristic. In addition, Applicants argue that claim 3 is not anticipated by the cited references since claim 3 requires that (1) the clones be prepared by using DNA from the uncultivated microorganism which has been recovered by selecting DNA with nucleic acid probes encoding a full length enzyme or a segment of an

enzyme, (2) the clones be further transformed with this probe-selected DNA and (3) expression products be obtained by expressing the library of clones. Applicants submit that Yen fails to suggest the claimed invention because in Yen's method, the isolated DNA was pretreated so as to bias the DNA towards a particular known enzyme with a restriction endonuclease whose active site was known to exist in some or all of the genes encoding the predetermined target enzyme. Furthermore, Applicant's argue that the Pm KR-1 cells of Yen et al. were all obtained from the same species of organism and thus are not randomly produced as is required in claim 1. In addition, it is Applicant's contention that Yen fails to suggest screening a library from a mixed population of uncultured organisms to determine those having a desired enzymatic property as is required by claim 3. Applicants argue that Yen knows in advance that all the molecules in the library to be screened are but mutants of a single known DNA.

In regard to More, Applicants contend that More does not cure the deficiencies of Yen since More, while describing the isolation of DNA from sediment samples containing a mixed population of microorganisms, it also teaches the amplification of a single predetermined gene, nahR, and only for the purpose of determining the performance efficiency of the DNA extraction procedures. According to Applicants, More also fails to suggest how a library from a mixed population of uncultured microorganisms would be prepared for screening to identify unknown DNAs encoding proteins having the desired enzymatic property. It is Applicant's opinion that even if one of skill in the art is motivated to combine the references, there is no reasonable expectation of success because neither reference teaches how to prepare a DNA library containing DNA from at least one uncultured (i.e. unknown) organism or from a mixed

population for screening to identify clones with DNA encoding an enzyme having a desired enzymatic characteristic.

21. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection as it applies to amended claims 1-3 or newly added claims 4-5 for the following reasons.

Claims 1-2, as amended, are still directed to a method for identifying clones of a recombinant library produced from DNA derived from uncultivated organisms which comprises screening the expression products of such clones in the liquid phase, wherein the DNA can be modified or mutagenized prior to transformation of the clones, with the exception that the expression product is now an enzyme. Claims 3-4 are directed to a method for identifying clones having DNA recovered from an uncultivated organism to identify any protein having any characteristic wherein the DNA from the uncultivated organism has been pre-selected prior to the preparation of the clones using specific probes and wherein the DNA can be modified or mutagenized prior to the preparation of the clones. Claim 5 is directed to the method of claim 3 wherein the characteristic being identified is pH stability, temperature stability or substrate specificity. See claim rejections under 35 112, second paragraph for claim interpretation.

As indicated in previous Office Action Paper No. 9, Yen et al. teaches a process for identifying clones of a recombinant P. mendocina KR-1 library wherein the clones are screened in the liquid phase for toluene monooxygenase activity using radioactive toluene (column 14, Example 11, Table I). As such, the limitation in claims 1-2 in regard to the expression product being an enzyme is taught by Yen et al. (i.e. monooxygenase).

In regard to the limitations in claims 3-5, Yen teaches the detection of monooxygenase activity by using several substrates and determining if phenolic compounds were formed (Column 15-16, Example 12, Table II), therefore substrate specificity was tested. As such, it would have been obvious at the time the invention was made to practice the method of Yen and More with DNA from uncultivated organisms which has been pre-selected by using a specific nucleotide probe for preparing the library of clones, mutagenize said DNA prior to its use in preparing the clones, and test for substrate specificity. A person of ordinary skill in the art is motivated to pre-select the DNA prior to preparing the clones, for the benefit of reducing the number of clones to be screened in the method. In addition, as indicated in previous Office Action Paper No. 9, one of skill in the art is motivated to mutagenize the DNA before preparing the clones to study the effect of mutations in the function of the corresponding protein and to further characterize the structure-function relationship in the protein. Furthermore, one is motivated to test for substrate specificity to further characterize the enzyme. One of skill in the art has a reasonable expectation of success at practicing the method of Yen and More with DNA from uncultivated microorganisms which has been pre-selected with a specific nucleotide probe prior to preparation of the clones since nucleotide probes which hybridize to DNA for detection/isolation are well known and widely used in the art. In addition, More et al. teaches PCR amplification of sediment-derived DNA (page 1576, column 1), which as known in the art, requires the use of probes (primers) which have to specifically hybridize to the DNA targeted for amplification. Furthermore, one of skill in the art has a reasonable expectation of success at practicing the method of Yen and More with DNA which is mutagenized prior to its use in the preparation of clones since Yen teaches mutagenesis of DNA to be used for preparation of

clones. One of skill in the art has a reasonable expectation of success at testing substrate specificity since Yen et al teach toluene monooxygenase substrate specificity with a variety of phenyl substrates. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

In regard to arguments that Yen's teachings fail to suggest the claimed invention because (1) the DNA was pretreated and therefore biased towards a particular DNA, and (2) Yen does not suggest screening a library from a mixed population of uncultured organisms, it is noted that the Examiner is not contending that the DNA used by Yen for the library of clones is that of the instant claims. Instead, the Examiner contends that one could use the isolated DNA from soil as taught by More, which is DNA from at least one uncultivated microorganism, as recited by the claims. In regard to arguments that the term "randomly produced" is not taught or suggested by Yen, it is noted that the term, as written, does not refer to the organisms from which the DNA is isolated but rather to the preparation of clones. In fact, the subsequent term, "DNA of at least one uncultivated organism", clearly indicates that the DNA may come from the same species of organism as long as it is not cultivated. Furthermore, it is noted that, as known in the art, transformation of clones with a DNA library, is inherently a random process since not all of the cells exposed to the DNA will be transformed, therefore the limitation "randomly produced" is taught by the method of Yen and More.

In regard to the teachings of More et al., while it is agreed that More amplifies a polynucleotide encoding the nahR gene product to test the performance of such DNA for PCR applications, More et al. teaches the isolation of DNA from soil which would have DNA from at least one isolated microorganism. Since this is the limitation which is lacking in the teachings of

Yen et al., the teachings of More et al. cure the deficiencies of Yen et al. in regard to the DNA used to produce the library of clones recited in the claims.

In regard to the expectation of success, the Examiner disagrees with Applicant's contention that there could not be a reasonable expectation of success at combining the references, since practicing the method of Yen with the DNA of More would only require changing the DNA used in the preparation of the library. Therefore, in view of the reasons of record and the reasons set forth above, the instant invention is rendered obvious by the method of Yen et al. and More et al.

Double Patenting

22. Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6280926 in view of More et al. (Appl. Environ. Microbiol. 60(5):1572-1580, 1994).

23. Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6168919 in view of More et al. (Appl. Environ. Microbiol. 60(5):1572-1580, 1994).

24. Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No.5958672 in view of More et al. (Appl. Environ. Microbiol. 60(5):1572-1580, 1994).

25. Claims 1-5 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 32-47 of copending Application No. 09/421629 in view of More et al. (Appl. Environ. Microbiol. 60(5):1572-1580,

1994). This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

26. Claims 1-5 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11, 14 and 16 of copending Application No. 09/467740 in view of More et al. (Appl. Environ. Microbiol. 60(5):1572-1580, 1994). This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

27. Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,528,249 (issued from Application No. 09/713176) in view of More et al. (Appl. Environ. Microbiol. 60(5):1572-1580, 1994). This is not a new double patenting rejection since the instant claims were provisionally rejected over claims 1-20, 23-25, 27-28 of then copending U.S. Application No. 09/713,176 in Paper No. 9, mailed on 12/27/2002. The subject matter of claims 1-25 of U.S. Patent No. 6,528,249 is the same as that of claims 1-20, 23-25, 27-28 of then copending U.S. Application No. 09/713,176. Therefore, the issues discussed in the corresponding provisional rejection as set forth in Paper No. 9 would apply herein.

28. Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,566,050 (issued from Application No. 09/861267) in view of More et al. (Appl. Environ. Microbiol. 60(5):1572-1580, 1994). This is not a new double patenting rejection since the instant claims were provisionally rejected over claims 1-5 of then copending U.S. Application No. 09/861,267 in Paper No. 9, mailed on 12/27/2002. The subject matter of claims 1-5 in U.S. Patent No. 6,566,050 is the same

as that of claims 1-5 of then copending U.S. Application No. 09/861267. Therefore, the issues discussed in the corresponding provisional rejection as set forth in Paper No. 9 would apply herein.

29. Claims 1-5 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No. 09/875412 in view of More et al. (Appl. Environ. Microbiol. 60(5):1572-1580, 1994). This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

30. These rejections, which have been discussed at length in Paper No. 9, mailed on 12/27/2002, were applied to claims 1-3 and are now applied to amended claims 1-3 and newly added claims 4-5 for the reasons of record and for the reasons set forth below.

31. Applicants traverse the instant rejections and submit that a terminal disclaimer has been filed disclaiming the terminal part of any patent that may issue on claims of the present application that would extend beyond expiration of any of the above issued patents and patents that may issue from the above co-pending applications. In view of the submission of the terminal disclaimer, Applicants argue that the cited patents and co-pending applications are not prior art against the present claims and that the teachings of More alone are not sufficient to render unpatentable the subject matter of the claimed invention.

32. As indicated above, the terminal disclaimer filed by Applicants is deemed defective since it disclaims a different application. As such, the terminal disclaimer does not obviate the double patenting rejections previously applied. While it is agreed that that the teachings of More alone do not anticipate the instant claims as written, the conflicting claims in U.S. Patent No.

6,280,926, 6,168,919, 5,958,672, 6,528,249 (previously Application No. 09/713,176), 6,566,050 (previously Application No. 09/861,267) and the conflicting claims in co-pending U.S. Application No. 09/421,629, 09/467,740, 09/875,412 render claims 1-5 of the instant application obvious in view of the teachings of More et al. for the following reasons.

Claims 1-2, as amended, are still directed to a method for identifying clones of a recombinant library produced from DNA derived from uncultivated organisms which comprises screening the expression products of such clones in the liquid phase, wherein the DNA can be modified or mutagenized prior to transformation of the clones, with the exception that the expression product is now an enzyme. Claims 3-4 are directed to a method for identifying clones having DNA recovered from an uncultivated organism to identify any protein having any characteristic wherein the DNA from the uncultivated organism has been pre-selected prior to the preparation of the clones using specific probes and wherein the DNA can be modified or mutagenized prior to the preparation of the clones. Claim 5 is directed to the method of claim 3 wherein the characteristic being identified is pH stability, temperature stability or substrate specificity. See claim rejections under 35 112, second paragraph for claim interpretation.

The limitation added to claims 1-2 in regard to the expression product being an enzyme, and the limitations recited in claims 3-5 in regard to the characteristic detected being an enzymatic characteristic such as substrate specificity, have already been addressed in Paper No. 9 since (1) in the method of claims 1-22 of U.S. Patent No. 6280926, the proteins being expressed are enzymes, (2) in the method of claims 3 and 9 of U.S. Patent No. 6168919, the DNA in the clones encode an enzyme, (3) in the method of claims 1-15 of U.S. Patent No. 5958672, enzymatic activity is detected, (4) in the method of claims 2-25 of U.S. Patent No.

6528249, enzymatic activity is detected, (5) in the method of claims 1-5 of U.S. Patent No. 6566050, enzymatic activity is detected, (6) in the method of claims 32-47 of copending U.S. Application No. 09/421,629, the biomolecule identified is an enzyme, (7) in the method of claims 11,14, 16 of copending U.S. Application No. 09/467740, enzymatic activity is detected, and (8) in the method of claims 1-22 of copending U.S. Application No. 09/875412, the clones express enzymes. It is noted that detection of enzymatic activity is required in the methods claimed in U.S. Patent No. 6,280,926, U.S. Patent No. 6,168,919, U.S. Patent No. 5,958,672, U.S. Patent No. 6,528,249, U.S. Patent No. 6,566,050, U.S. Application No. 09/421,629, U.S. Application No. 09/467,740, and U.S. Application No. 09/875,412. Since enzymes are specific for a particular substrate and the detection of enzymatic activity requires testing substrates to determine if the enzyme acts on them, substrate specificity is tested. Therefore, for the reasons set forth in Paper No. 9 and the reasons set forth above, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Conclusion

33. No claim is in condition for allowance.

34. Applicant's amendment of claims 1-3 and addition of claims 4-5 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

35. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

36. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

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